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THE SIMPLE ESTERASES OF HUMAN SKIN.

G. H. FINDLAY.

Section of Dermatology, Department of Medicine, University of Chicago.

THE simple skin esterases discussed here are those that act on esters of short chain fatty acids. They differ from the lipases, which act on esters of long chain fatty acids and behave otherwise towards activators and inhibitors.

Agnes Porter (1916) first demonstrated that human skin could hydrolyse tributyrin, the ester of a short chained fatty acid, by enzyme action. The features of this activity were further studied by others, although their methods were somewhat insensitive and the results not always conclusive by later standards (Sexsmith and Petersen, 1918; Wohlgemuth and Nakamura, 1926; Melcer, 1927).

Thompson and Whittaker (1944) initiated several recent studies on skin esterases which have been reviewed and extended by Magnus and Thompson (1954). Skin cholinesterases were found to be peculiar in acting very slightly on esters of short chain fatty acids. Hydrolysis of these esters was shown to be attributable almost entirely to an enzyme other than cholinesterase, and perhaps to a plurality of enzymes.

In testing simple esterase activity the more commonly selected alcoholic moieties in the ester may conveniently be substituted by naphthol. One may then use the liberated naphthol as a sensitive measure of hydrolysis both biochemically and histochemically by means of azo coupling. Nachlas and Seligman (1949a) introduced these naphtholic substrates, and Gomori (1953) has applied and simplified the methods. In the present study, Gomori's techniques essentially were used.

MATERIALS AND METHODS.

Normal fresh human skin was obtained from one breast and three mid-thigh surgical amputation specimens. Adjacent areas of these skin flaps were suited to histochemical and biochemical comparisons.

For the *biochemical* studies the subcutaneous fat was scraped off. Then epidermis and corium were together snipped into tiny fragments with scissors. Two hundred mg. quantities of these fragments were homogenized at about 5° C. in 10 ml. 0.2 M phosphate buffer pH 7.1 in a Potter-Elvehjem glass homogenizer. This gave a 2% homogenate which was frozen and thawed four times, centrifuged, and the chilled supernatant fluid rapidly filtered. The resulting clear extract was made up once again to 10 ml. volume, divided in smaller quantities among separate bottles and kept frozen until required.

Isolated epidermis was prepared by stripping it in ribbons off the stretched corium with a razor blade. A 10% extract was made in a way otherwise similar to the above procedure.

For the *histochemical* studies, some tissues were prepared by the usual method for esterase demonstration using acetone fixation and double imbedding in celloidin and paraffin (Gomori, 1952). Other portions of the tissues were fixed in chilled neutral formalin for 12 hours, washed in running tap water for 24 hours, infiltrated with 10% gelatin in 50% glycerin at 37° C. for 4 hours, refixed in chilled neutral formalin for 12 hours and cut on the freezing microtome.

As *substrates* eleven α -naphthyl esters of straight chain saturated fatty acids with 2–12 carbon atoms were used. For simplicity these will be referred to by the symbol α followed by a digit representing the number of carbon atoms in the fatty acid. Thus, $\alpha 4$ would represent α -naphthyl butyrate, for instance.

Most of these esters were not commercially available and were synthesized either directly from the corresponding acyl chloride or indirectly from the fatty acid *via* the acyl chloride. The fatty acids were converted to the acyl chlorides by using phosphorus trichloride. The esterification was carried out by adding an excess of the acyl chloride to α -naphthol in a small volume of pyridine, heating, and then pouring the liquefied mixture into cold water from which the water-insoluble ester-containing fraction was taken up into petroleum ether. This fraction was well washed and then chromatographed on an aluminium oxide column. The ester was eluted with petroleum ether, and was recovered usually as an oil at room temperature, which was colourless and free from naphthol. Stock solutions of these esters, 1% w/v in acetone, were kept in the ice chest.

In the *biochemical* tests, 5 ml. of a buffered substrate solution and 0.1–0.5 ml. of the skin extract were placed in photometer tubes and incubated in a water-bath at 37° C. After a chosen lapse of time (10–60 minutes), the free naphthol was azo-coupled in the presence of a detergent, the purpose of the latter being to prevent precipitation of the azo dye, and the optical density of the solution measured in a Coleman spectrophotometer. A graph previously prepared gave the conversion factor of optical density into micrograms of α -naphthol under corresponding conditions.

The substrate mixture used above contained 0.2 mM substrate, added from the 1% stock solution in acetone, 0.04 M phosphate buffer pH 7.1, and in some experiments, 25% by volume of propylene glycol as well (see below), in distilled water. This mixture was made freshly for each experiment. The coupling mixture, of which 1 ml. was added to each tube, contained about 50 mg. Red ITR Salt (diazotized 4-diethylsulphonamido-2-aminoanisole) in 10 ml. of a 3% solution by weight of Brij-35 (polyoxyethylene lauryl alcohol) in distilled water.

On removing the photometer tubes from the water-bath, it was found most practicable to add the coupling mixture and read the optical density immediately. Coupling was prompt, and constant values were thus obtained. Delay in reading the optical density led to deviation of the colour intensity up or down the scale

depending on the temperature and the proportions of practically every substance in the solution.

Photometric readings were taken at $550\text{ m}\mu$, the point of maximal optical density of the azo dye.

In some experiments propylene glycol was included in the substrate mixture. Komori (1953) introduced propylene glycol as an aid to dissolving the longer chain esters, but it was also found by him to be an activator of esterase.

For keeping the hydrolysis within a convenient range, the extract made from 5 mg. of skin was required for each test.

In all the biochemical tests, proper controls were always necessary, since the apophtholic esters undergo a variable spontaneous decomposition during the tests.

For the *histochemical* tests, a solution was used containing approximately 0.2 mM of the substrate, a few ml. phosphate buffer of pH 8 and about 50 mg. Diazo Blue B salt (tetrazotized diorthoanisidine) to 50 ml. This mixture was rapidly filtered and cooled, and the sections kept in it until staining was adequate. The solution was re-filtered if it became turbid.

BIOCHEMICAL RESULTS.

It was established that with all substrates from $\alpha 2$ to $\alpha 11$, the rate of hydrolysis with skin esterase was constant over 10-minute intervals for the first hour. The rate of hydrolysis was also proportional to the amount of skin extract used.

Fig. 1 shows the relative rates of hydrolysis of the homologous series of esters from $\alpha 2$ to $\alpha 12$ by esterases of the skin. The chain length of the fatty acid moiety is plotted against an arbitrary scale representing the initial velocity. When no propylene glycol was used, there was an increase in velocity up to $\alpha 4$ followed by a decline to $\alpha 8$. When propylene glycol was present in the substrate mixture, an activation of hydrolysis was noted with all substrates. This activation increased with the chain length up to a maximum at $\alpha 7$, and displaced the peak of the curve from $\alpha 4$ to $\alpha 5$. The changes in velocity with ester chain length were not smooth. A zig-zag curve was noted which showed that the even numbered esters were relatively better hydrolysed in the ascending segment of the curve from $\alpha 2$ to $\alpha 5$, and the odd numbered esters in the descending segment from $\alpha 5$ to $\alpha 12$.

A single experiment was done in which β -naphthol replaced α -naphthol in the ester substrate. α -naphthyl butyrate was found to be hydrolysed six times faster than β -naphthyl butyrate.

In another experiment the hydrolysis of an unsaturated fatty acid ester was compared with that of its saturated analogue. α -naphthyl undecanoate was hydrolysed at two-thirds of the rate of α -naphthyl undecylenate.

The absolute rates of hydrolysis were determined for all the skin samples, using $\alpha 4$ at pH 7.1, without propylene glycol, at 37°C . It was found that $0.015\text{--}0.065\text{ }\mu\text{M}$ of $\alpha 4$ were hydrolysed per hour by the extract of 1 mg. of skin. The lowest value was obtained from the skin of a leg amputated for thrombotic arterial disease.

Isolated epidermis was found to be about five times more active enzymatically than combined epidermis and corium from the same source. Three tests were done which demonstrated this. With $\alpha 2$ and $\alpha 5$ the hydrolysis by epidermis and corium was 18% of the value given by epidermis alone, and with $\alpha 8$ it was 28%.

A few tests were conducted on the relative rates of hydrolysis with skin (epidermis plus corium) from the foot sole. The pattern was found to agree with that given in Fig. 1.

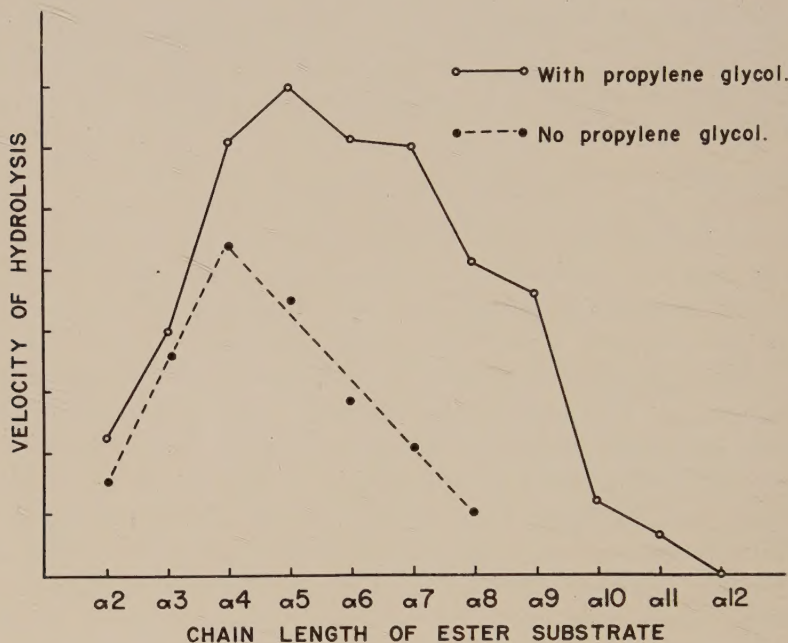


FIG. 1.—Graphs showing the action of skin esterase on a series of esters.

The inhibitory effect of several substances was tested on the enzyme activity with $\alpha 2$, $\alpha 4$, $\alpha 5$ and $\alpha 8$. At concentrations of approximately 1×10^{-4} M eserine salicylate, the enzyme activity fell by 20–25%. Bile salts (0.004 M sodium taurocholate) produced 75–80% inhibition. Atoxyl (0.002 M sodium arsanilate) produced 30% inhibition. Quinine (1×10^{-4} M quinine base), mepacrine (1×10^{-5} M atabrine dihydrochloride) and Prantal (0.0025% diphenmethanil methylsulphate, Schering) were without any effect on the hydrolysis of $\alpha 5$ in the presence of propylene glycol.

HISTOCHEMICAL RESULTS.

A preliminary experiment was conducted to study the effects of acetone and formalin fixation on skin esterases. Of three adjacent pieces of skin,

the first was fixed in chilled acetone, the second in chilled neutral formalin and the third kept as a control. Fixation lasted 12 hours, after which the formalin fixed specimen was washed in running tap water for a further 24 hours. All three specimens were homogenized and extracts prepared in the way described above. Acetone fixation had reduced the esterase activity by 30 to 60%, the greater inhibition being with the shorter chain esters. Formalin produced 80-85% loss of activity.

Despite the promise of acetone fixation suggested by these findings, acetone fixed *imbedded* skin showed no esterase activity histochemically. This confirmed the experience of Nachlas and Seligman (1949b). Fortunately, however, the formalin fixed *frozen* sections showed a fairly well-retained activity, and the ensuing findings are based on sections prepared in this way. As histochemical substrates $\alpha 2$ and $\alpha 4$ were used. The results were somewhat similar and the descriptions are therefore combined. A few additional observations were made with two other esterase substrates, namely the acetate and the chloroacetate of *Naphtol AS*. *Naphtol AS* is the anilide of 2-hydroxynaphthoic acid.

The cytoplasm of all cells in the *Malpighian layer of the epidermis* showed diffuse esterase activity (Figs. 2 and 3). Slightly greater activity was noted around the sweat ducts. Intercellular spaces were free of esterase. The *stratum corneum* frequently showed a dense concentration of esterase in its deepest part, where the keratinizing cells lose volume and lose their nuclei abruptly (Fig. 2). This was not invariable, since the stratum corneum was also found in places to be entirely negative, diffusely positive or provided with a positive band in a position other than that of the basal horny layer. Such bands were found in the outer mature keratin layers and in the outer part of the stratum lucidum on the sole of the foot (Fig. 3).

Epidermal *melanoblasts* and dermal *chromatophores* could not be shown to react any differently from the cells surrounding them. *Naphtol AS* chloroacetate occasionally produced a little reaction in dendritic epidermal melanoblasts.

In the *hair follicles* the outer root sheath was moderately reactive throughout. However, the inner edge of the inner root sheath, and the epithelial linings of the hair canal up to the surface were often strongly reactive. *Sebaceous cells* were themselves not reactive, but the basal cells of the sebaceous glands did react.

Eccrine sweat gland acini were strongly reactive, particularly with $\alpha 2$ (Fig. 4). The myoepithelium could not be separately identified. The duct cells also contained much esterase, and showed as a rule a clear increase in activity towards the free edge of the duct epithelium (Figs. 2 and 4). In their entire course through the stratum corneum on the sole of the foot the sweat ducts were lined by a layer of cuticular cells which showed a clear esterase reaction,

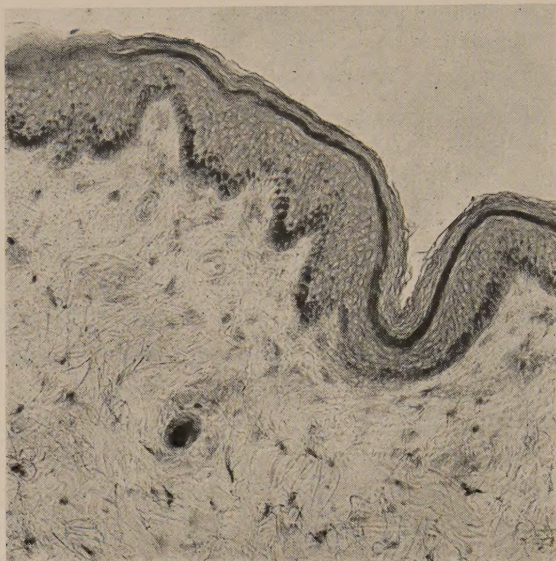


FIG. 2.—*Distribution of simple esterase in normal human skin from the leg (Negro).* Esterase activity in cytoplasm of Malpighian layer, and a strong band in the basal horny layer. A sweat duct in corium stains strongly, and stellate cells in the corium are also seen. Esterase activity shows as grey to black, though melanin and some fibrils appear dark, the latter because of diffraction. Frozen section: α -naphthyl butyrate and Diazo Blue B without counterstain.

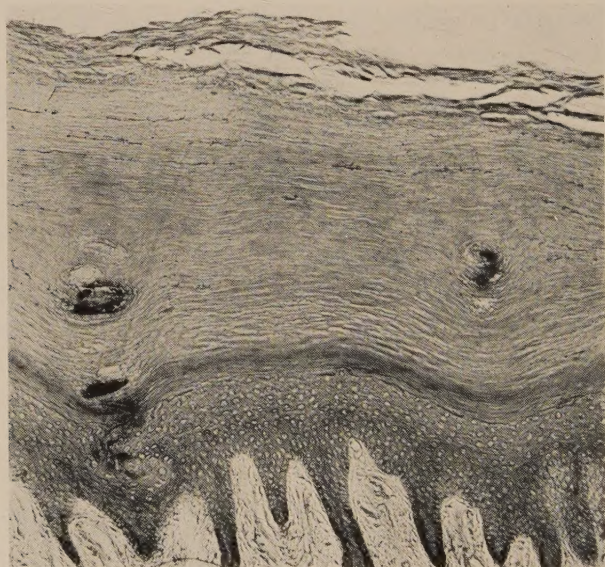


FIG. 3.—*Sweat ducts in the sole of the foot.* Cells bordering the eccrine sweat ducts show esterase reaction. Activity also noted in the stratum Malpighii and stratum lucidum. The stratum corneum shows some dark diffraction lines that do not represent esterase. Frozen section: α -naphthyl butyrate and Diazo Blue B without counterstain.

Contrasting with the surrounding horny cells (Fig. 3). The same features were noted, though less conspicuous, in areas with a thinner stratum corneum. A single specimen of axillary skin treated with Naphtol AS acetate showed positively reacting cells, singly and in groups, in the *apocrine gland* acini. Cellular elements in the *corium* showed esterase activity in their cytoplasm. With $\alpha 4$ most of the cells reacted in some degree, but it seemed that $\alpha 2$

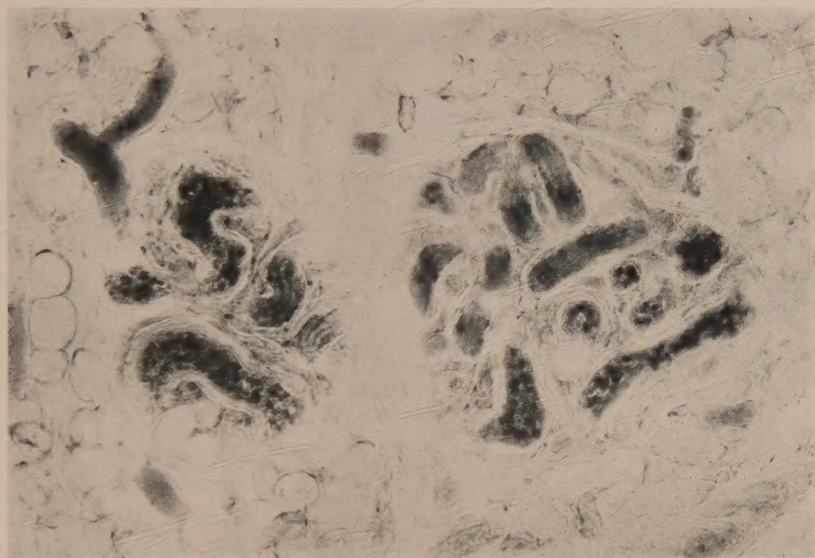


FIG. 4.—Esterase in eccrine sweat gland from the sole. Cloudy esterase activity in acinar cells and in some sweat duct segments, the latter showing greater esterase reaction in cells towards the lumen along the cuticle. Edges of some fat cells show esterase reaction. An engorged venule is seen in the top left. Frozen section: α -naphthyl acetate and Diazo Blue B without counterstain.

displayed no more than about a fifth of the cells present (Fig. 2). With these substrates, and with Naphtol AS acetate as well, the peripheral extensions of many cells were well revealed, frequently dendritic, with complicated and wide ramifications. In many cells cytoplasmic granules were seen which closely resembled mast-cell granules. Other sites of esterase activity were also granular, though the granules were sparse and variable in size and distribution. Other cells showed non-granular esterase reactions, often confined to the perinuclear area. Some cells showed clearly striate areas of reaction in the cytoplasm. Fat cells showed the presence of esterase in the tiny strips of cytoplasm around the fat droplets.

Vascular endothelium, adventitial cells, pericytes and glomus cells were inactive. Basement membranes and fibrous elements in the dermis were without esterase activity.

COMMENT.

Gomori (1953) has published the relative rates of hydrolysis of a number of short chain α -naphthyl esters by esterases of the human liver, pancreas, blood serum and urine. The biochemical properties of skin esterase were found in the present study to be altogether different from those of the tissues and fluids just mentioned, in respect of substrate preferences and reactions to activators and inhibitors. For details, Gomori's paper should be consulted. These features establish the uniqueness of the skin enzyme as far as present information permits. Moreover, the esterase concentration in the skin was about a thousandth of that in the pancreas or liver.

For biochemical purposes it was convenient to consider skin esterase activity as an entity, but the histochemical results show the complexity of the material that is pooled in the extract of whole skin. Esterase was present in virtually every cell type, although the reactivity with different substrates produced varying histological pictures. Esterase appeared particularly to be concentrated in "lifeless" cell derivatives on surfaces, such as in the cell relics in the basal horny layer, the sweat duct cuticle and the cuticle of the inner root sheath. The high concentration of esterase in the cells bordering the sweat ducts in their passage through the stratum corneum supports the view of Pinkus (1939) that these cells differ from the surrounding horny cells.

The cells in the corium showed esterase activity in the cytoplasm at some distance from the perinuclear area. This caused many of them to reveal a system of dendrites which are invisible in ordinary histological sections. Chessick (1954) mentioned these dendritic cells in esterase studies of the tongue of the rat, but could not settle their identity. Either these cells include fibroblasts with hitherto unsuspected morphological and functional peculiarities, or else they include mast cells, various "neural" cells, pericytes, etc., that normally masquerade in large numbers as fibroblasts. Some of these problems of cell identification in the corium were discussed in a previous communication (Findlay, 1953).

No notable effects on the esterase activity of the skin were elicited by the drugs tested. Furthermore, the significance of these esterases in disease is still quite unknown. Their high concentration near all skin surfaces, however, suggests that the esterases may play a role in the integrity of cutaneous ducts or in the shedding of keratin.

SUMMARY.

The simple esterases of normal human skin were studied biochemically and histochemically, using the same substrates for both procedures. These substrates were the esters of α -naphthol with short chain fatty acids containing

12 carbon atoms. Skin esterase was found to possess affinities for ester substrates which were significantly different from the known substrate preferences of human liver and pancreatic esterase, and the esterases of human blood serum and urine. Esterase was approximately a thousand times more concentrated in the liver and pancreas than in the skin.

Failures to demonstrate simple esterases in the human skin histochemically are found to be due to a sensitivity of these enzymes to the processes of tissue imbedding. The enzyme activity was preserved in frozen sections. The cytoplasm of all cell types in the skin showed some measure of esterase activity, but high concentrations were seen only along the borders of the epithelia, suggesting a possible importance of the enzymes in epithelial squamation. In the corium the peripheral dendritic processes of many connective tissue cells showed esterase activity, thus making visible some regions of the cytoplasm that are seldom seen by usual staining techniques. In cholinesterase could not have been responsible for the hydrolysis of the ester substrates used, since the hydrolysis was not greatly inhibited by eserine. Neither could the enzymatic activity be ascribed to lipases, because the esters containing longer chain fatty acids were progressively less well hydrolysed, and the enzyme action was also markedly inhibited by bile salts. Quinine, papaverine, atoxyl and Prantal were tested for their effects on skin esterase, but no gross alterations in enzyme activity were caused by these substances. The wider relations of these enzymes to the health, disease and therapeutics of the skin remain unexplored.

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“PEMPHIGOID” (PARA-PEMPHIGUS): ITS RELATIONSHIP TO OTHER BULLOUS DERMATOSES

J. R. PRAKKEN AND M. J. WOERDEMAN.

From the Department of Skin and Venereal Diseases, University of Amsterdam
(Head: Prof. Dr. J. R. Prakken).

RECENTLY the terms “bullous pemphigoid” (Lever, 1953) and “pemphigoid” (Rook and Waddington, 1953) were adopted for a bullous dermatosis which clinically sometimes closely resembles pemphigus vulgaris and which is characterized histologically by subepidermal bullae without acantholysis, as is seen in Duhring’s dermatitis herpetiformis. However, it has been clearly shown by Lever and by Rook and Waddington that pemphigoid differs from both these dermatoses in many ways. We are convinced that the separation of pemphigoid from the other bullous dermatoses is justified.

In our opinion both terms “bullous pemphigoid” and “pemphigoid” are not well chosen. They may cause confusion as the term “pemphigoid” is already widely used as a synonym of impetigo bullosa neonatorum or staphylo-dermia bullosa disseminata neonatorum, and Touraine (1954) uses it to indicate all bullous dermatoses which are not classified in the pemphigus group. We agree with Rook and Waddington that “bullous pemphigoid” is a pleonasm. We suggest the name “para-pemphigus” but will use in this paper the term “pemphigoid”, as has been done by Rook and Waddington.

This paper is based on a study of 66 bullous eruptions of which 11 were pemphigus vulgaris, 19 pemphigoid (of which in 4 cases the diagnosis could not be established with certainty) and 21 dermatitis herpetiformis. These patients were treated from 1947 onwards. In addition a few cases of pemphigus foliaceus, pemphigus vegetans, pemphigus erythematosus (Senear-Usher), Hailey and Hailey’s disease, granuloma eosinophilicum pemphigoides and herpes gestationis were studied.

In the histological investigation special attention was paid to the situation of the bullae and the occurrence of acantholysis. We therefore made as many serial sections as possible and preferably small bullae were excised in an early stage of their development; in some patients biopsies were performed in different stages of the disease.

In general our conclusions as regards pemphigoid are in agreement with those of Lever and of Rook and Waddington. We were able to confirm Rook and Waddington’s observation that in many cases of pemphigoid the lesions

were localized to one region for some months before the eruption generalized. In 7 of our 19 pemphigoid patients the disease was at first localized to one region for from 1 to 18 months.

Three of our pemphigoid patients were children, 2, 3 and 4 years old at the onset of the disease.

The results of our investigation and those of Lever and of Rook and Waddington differed on two points—the mortality rate, and the anomalous histological findings in three patients of ours who were diagnosed as pemphigoid.

Rook and Waddington reported 12 fatal cases of their 38 pemphigoid patients and Lever calculated a mortality rate of 24%, whereas only 3 of our 19 patients died, aged 84, 74 and 68 years. All our patients have been followed for a year or more. This difference in mortality rate is probably brought about by the ACTH and cortisone therapy which was given in 11 of our 19 pemphigoid patients, whereas Lever's and Rook and Waddington's patients were not treated with these hormones because they were not available at that time. Although our 3 fatal cases also had ACTH and cortisone treatment, the other 8 patients were influenced favourably.

The most striking example is a man aged 65, who was one of the first of our patients treated with steroids. He was admitted to the hospital in a serious condition with many blisters. His general condition deteriorated every day and he was almost moribund when treatment was started. The dosage was low, 24 mg. ACTH intramuscularly daily, but already after two days his condition had much improved. After 2 months' treatment with ACTH intramuscularly and cortisone orally, with a gradually lowering dosage from 24 mg. ACTH daily, the patient was discharged in excellent health and with a normal skin. The itching which was still present on discharge disappeared after a month. During the last 2½ years, this patient has had no more symptoms of his disease.

Of the 4 patients in whom the diagnosis of pemphigoid could not be made with certainty, we could not exclude a toxicodermia in one case; in the other 3 the histological findings were not typical either of pemphigoid or of pemphigus vulgaris. In two of these patients we observed in the same section both intra-epidermal and subepidermal bullae without acantholysis. The situation of the bullae was confirmed in serial sections, and it can be assumed that in these two patients subepidermal and intra-epidermal bullae occurred simultaneously. In one of these two patients the clinical aspect and the course of the disease were typical of pemphigoid; the other patient, a man aged 68, presented a clinical picture which was typical of pemphigus vulgaris. However, in many serial sections and scrapings of the floors of bullae acantholytic cells were never seen. The course was lethal in a few months. In the third patient, a woman aged 52, who clinically appeared to be a typical case of pemphigoid, the histological investigation showed intra-epidermal bullae without acantholysis. We were not able to study serial sections of this patient and therefore do not know whether subepidermal bullae were also present.

Lever consistently found subepidermal bullae without acantholysis in his 44 cases of pemphigoid. A few times he saw intra-epidermal bullae which in serial sections appeared to be extensions of subepidermal bullae. Rook and Waddington reported no anomalous histological findings in their cases of pemphigoid. On the basis of our findings in the three latter patients, however, it is our opinion that in a small number of cases pemphigoid and pemphigus vulgaris cannot be separated absolutely, even on extensive histological investigation.

In this respect the observation of Hellier (1954) is of great importance. In the case of a woman aged 69, he performed three biopsies within two years. When the first two biopsies, which showed subepidermal bullae without acantholysis, were performed, the patient presented a severe bullous eruption clinically typical of pemphigus vulgaris. When the third biopsy was done, the clinical picture was that of pemphigus erythematosus (Senear-Usher); the histological section then showed an intra-epidermal bulla with acantholytic cells.

Nelemans (1951) raised the question whether in different phases of pemphigus vulgaris the bullae would always be situated at the same level. In a number of patients we performed biopsies at different times. In most cases all histological sections were essentially the same, but in one patient suffering from typical herpes gestationis we observed in the serial sections an intra-epidermal bulla without acantholysis and after two weeks a subepidermal bulla without acantholysis.

On the basis of Hellier's observations and our own findings, therefore, the possibility must be taken into account that intra- and subepidermal bullae may occur in the same patient simultaneously or successively in different phases of the disease.

During the histological investigation we made a few observations which we will report here briefly.

In the histological sections of a patient whose clinical aspect and course were typical of pemphigoid, we observed subepidermal bullae while we were in doubt whether acantholysis was present (Fig. 1). The intercellular bridges of the epidermal cells at the epidermo-dermal border are broken off by the pressure of the subepidermal bulla, but there are no well-marked degenerated, acantholytic cells. In our opinion we see here a process which has been called "desmorhexis" by Brennan (1953) and which must be distinguished from acantholysis.

In two typical cases of dermatitis herpetiformis there were anomalous histological findings. In one case we observed in the serial sections intra-epidermal bullae, but without acantholysis. This has been described a few times (Dupont and Piérard, 1949; Lapière, van Runkelen and Dussart, 1946). In the other patient, who had suffered from dermatitis herpetiformis for more than nine years, we saw in the serial section subepidermal bullae and acantholysis (Fig. 2). Fassotte (1948) reported a fatal case of pemphigus vulgaris

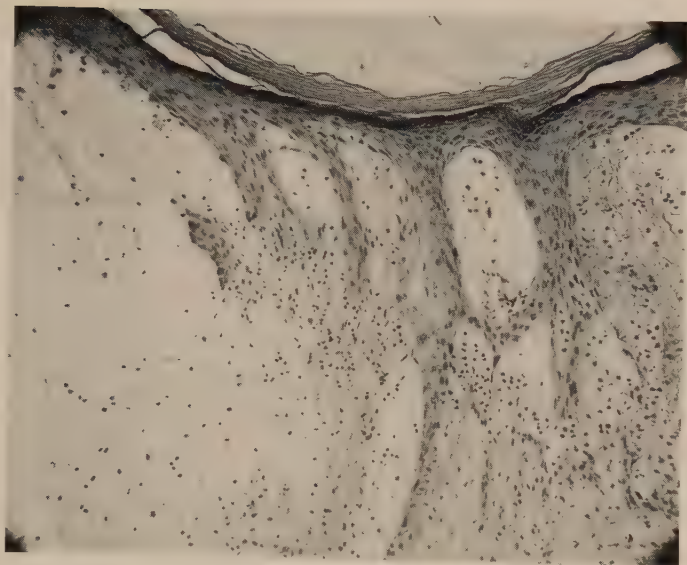


FIG. 1.

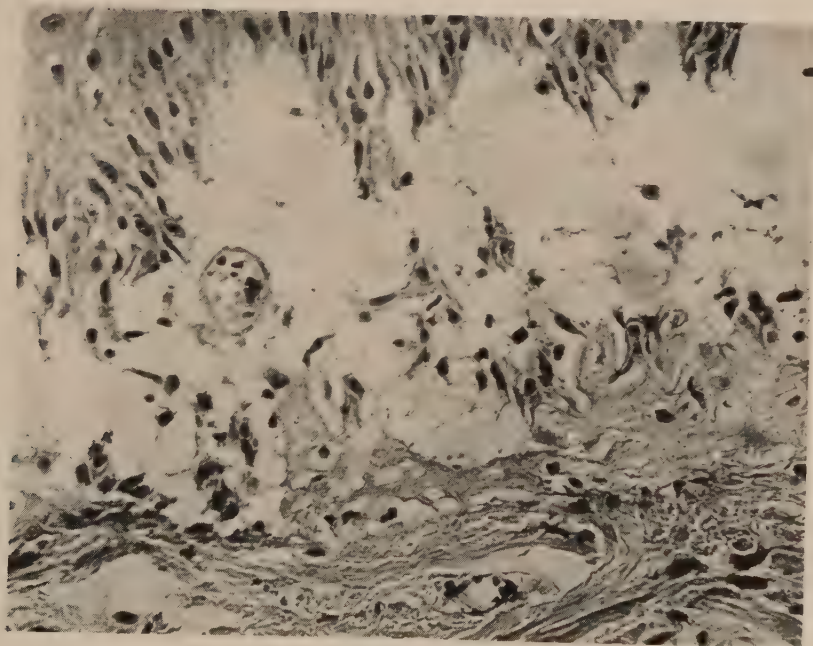


FIG. 2.

with subepidermal bullae and acantholysis, but as far as we know this histological picture has never been described in a case of dermatitis herpetiformis.

DISCUSSION.

In making the diagnosis of pemphigus vulgaris or pemphigoid according to histological criteria (intra-epidermal bullae and acantholysis in pemphigus vulgaris and subepidermal bullae without acantholysis in pemphigoid) we were unable to make a definite diagnosis in three cases in spite of extensive histological investigation. This is not surprising, since it appears from Hellier's publication and our own findings that a patient with a bullous dermatosis may have intra- and subepidermal bullae simultaneously or successively in different phases of the disease. Moreover, in a case that was clinically typical of pemphigoid, we observed intra-epidermal bullae without acantholysis, and a case of Duhring's dermatitis herpetiformis showed an identical histological picture. Another case of classical dermatitis herpetiformis showed subepidermal bullae and acantholysis.

On the basis of the above evidence it is our opinion that in general more value should be attached to the clinical picture than has been done in the years following Civatte's (1943) publication. In spite of the fact that in a small number of cases pemphigus vulgaris, pemphigoid and dermatitis herpetiformis cannot be separated absolutely, we feel that it is still justifiable to separate pemphigoid (para-pemphigus) from the other bullous dermatoses on account of its different clinical picture and course. The incidence of pemphigoid (para-pemphigus) seems to be higher than that of pemphigus vulgaris. The problem remains whether pemphigoid has to be considered as a variety of dermatitis herpetiformis, for which the analogous histological picture is a strong argument. Perhaps one may get nearer to a solution through electron-microscope studies of the collagen in pemphigoid, as has been done in pemphigus vulgaris and dermatitis herpetiformis by Everall and Reed (1953) or in studying the tonofibrillar system as has been done by Nieuwmeyer (1953) and others. It must also be considered whether pemphigoid is a variant of pemphigus vulgaris or perhaps of erythema multiforme. Probably, however, the solution will only be reached when the aetiology of these bullous dermatoses has been discovered. It is quite possible that pemphigoid will turn out to be a syndrome with more than one cause, as has been suggested by Rook and Waddington.

SUMMARY.

This paper is based on a study of 66 bullous eruptions of which 19 were pemphigoid. In 3 of these 19 cases the differential diagnosis between pemphigoid and pemphigus vulgaris could not be made with certainty in spite of exten-

ve histological investigation. It is the authors' opinion that in a small number of cases pemphigus vulgaris, pemphigoid and dermatitis herpetiformis cannot be separated absolutely.

Anomalous histological findings are reported in two cases of Duhring's dermatitis herpetiformis and in one case of herpes gestationis.

Intra- and subepidermal bullae may occur simultaneously as well as successively in different phases of a bullous disease, and more value should be attached to the clinical picture than has been done in recent years.

The use of the term “ pemphigoid ” in the sense of Lever and of Rook and Waddington is inadvisable as it is already used for a quite different condition (impetigo bullosa neonatorum). The term “ para-pemphigus ” is suggested.

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THE AREA FACTOR IN THE IRRADIATION THERAPY OF WARTS.

R. G. PARK, M.D., M.R.C.P.,
Dermatologist, Wellington Hospital, N.Z.

COMPARED with other methods of local destruction, x-ray therapy is a painless and convenient means of treating the common wart. Yet it has never found widespread favour because of the low proportion of cures it achieves. Any technique, therefore, which increases the proportion of successes with this measure is to be welcomed.

The standard method is usually to give a full skin dose of radiation to the wart, and if it does not disappear in a month or six weeks, to give the same or an increased dose as a final treatment. Thus, MacKee and Cipollaro (1946) advocate an initial treatment of 300 r and a second one of 300-600 r.

These figures are based on the fact that 300 r is the skin erythema dose for unfiltered low-voltage radiation. However, the work of MacKee, Cipollaro and Mutscheller (1943) has shown that this applies only to areas of about four square centimetres or more. Smaller areas require progressively more x-ray to cause the same biological effect, because the back-scatter produced in them is less. They found that this variation follows a mathematical pattern, and can be expressed by the formula

$$r_s = k \frac{m}{m - 2b}$$

where r_s is the dose required to cause erythema, m is the diameter of the diaphragm opening shielding the lesion, b is the diameter of the marginal zone referred to below, which for low-voltage radiation is 1.5 mm., and k is the dose of x-ray required to cause erythema in large fields (300 r for low-voltage radiation).

Since most warts are of these smaller sizes, it should be possible to give them higher doses without undesirable reactions. The purpose of this investigation has been to test the results of treatment based on these findings. It was considered reasonable to deliver to each wart a full skin dose repeated after an interval of two weeks, a method which has been used successfully for plantar warts (Montgomery and Montgomery, 1941). The erythema doses, calculated according to the formula above, were as follows :

Diameter of field (mm.).	Dose. (k = 300).
20 . .	350
12 . .	400
10 . .	430
9 . .	450
8 . .	480
7 . .	525
6 . .	600
5 . .	750
4 . .	1200

MacKee, Cipollaro and Mutscheller found that when an area is shielded with lead, there is a margin of 1.5 mm. which does not receive the full dose of the radiation, and it is necessary to place the shield this distance outside the edge of the lesion. This principle was followed in the present series, and the smallest lesions of 1 mm. diameter were treated through an aperture of 4 mm.

There were two sets of controls. The first was treated by the standard method mentioned above. Since it has even been suggested that any success from x-ray therapy in warts is due to the psychological effect (Goldsmith, 1936), a second control series was included in which the warts received no effective radiation. In order to eliminate any variations due to suggestion, all cases of warts seen at the skin clinic during the period of the investigation which were thought suitable for irradiation were treated ostensibly by the same routine. They were given treatments at 0, 2, 4, 8 and 12 weeks, by the following methods in strict rotation :

- (i) The first and second treatments were erythema doses corrected as above for area. The other treatments were the same, but " filtered " with 2 mm. of lead.
- (ii) The first treatment was 300 r, the third 300-600 r, and the remainder 900 r " filtered " with lead.
- (iii) All doses were 300 r " filtered " with lead.

The apparatus used was a Philips contact therapy plant, operating at 50 kv and 2 ma, F.S.D. 4 cm. All treatments were given personally by the writer, the variations in dosage being known only to himself. No dogmatic prognosis was given, and the patients were simply told that up to five doses would be given, and if the warts had not disappeared by then, they would be treated otherwise. If they had cleared before the five doses had been completed, no more treatment was given. The reason for the fourth and fifth " doses " (with no effective radiation in all series) was to ensure that patients remained under observation long enough to judge the results.

LATE EFFECTS.

Patients have been seen both from this series and from a larger number treated in private practice by method (i), up to three or four years afterwards.

RESULTS.

	Method.		
	(i).	(ii).	(iii).
Cases treated	15	15	15
Defaulted	3	2	2
Completed treatment	12	13	13
Number of warts treated	32	43	59
Number cleared	21	14	14
Percentage cleared	66	33	24
Difference from control (%)	42	9	—

In no case have there been any radiation sequelae at the site of warts which had responded to treatment.

SUMMARY.

In a series of common warts treated by x-ray 24% disappeared in controls which received no effective radiation, 33% disappeared after treatment by a standard textbook method, and 66% disappeared after treatment by a method of intensified dosage within the limits of safety.

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NON-FLUORESCENT *MICROSPORUM AUDOUINI* AND *CANIS* INFECTIONS OF THE SCALP

MARTIN BEARE, M.D., M.R.C.P.,

Assistant Physician, Skin Department, Royal Victoria Hospital, Belfast : Assistant Dermatologist,
Royal Belfast Hospital for Sick Children,

AND

JACQUELINE WALKER, Ph.D.,

Mycological Reference Laboratory, Public Health Laboratory Service,
London School of Hygiene and Tropical Medicine.

ONE of the most useful aids to diagnosis in the whole field of medicine is the Wood's light test for hairs infected by species of *Microsporum*. In practice and within its limitations the test may be regarded as specific. When one considers the large outbreaks of tinea capitis due to these microspora and the detail with which the cases have been studied in recent years it is remarkable that—as far as we can discover—there has been no mention of nonfluorescence in either *Microsporum audouini* or *Microsporum canis* infections. Some authors have recorded decrease in brilliance of the fluorescence as infection clears spontaneously (Beare and Cheeseman, 1951 : Kligman, 1952 : Whittle, 1953), and Davidson and Gregory (1932) describe a case which showed only a transient purple-green fluorescence, but there is no record of any case which was non-fluorescent from outset to recovery. The rarity of the event is praised indeed for the specificity of the Wood's light test.

CASE REPORTS.

CASE 1.—A boy aged 9 was seen on 22.xi.50 with a small non-inflammatory patch of tinea capitis on the occiput. The duration given was three weeks. He was subsequently seen at 7–14-day intervals until 15.iii.51. Mycological examinations of hair were made on a number of occasions. On 22.xi.50 and 21.xii.50 *M. audouini* was isolated but subsequently there was no growth. He was regarded as clinically clear on 25.i.51. Treatment included local applications of salicylic acid and sulphur ointment (NF) and later tincture of merthiolate. At no time during any of his attendances was fluorescence observed under Wood's light and manual epilation of bumps in the peripheral parts of the patch never revealed any intrafollicular fluorescence.

One of us (J.W.) has seen five cases, in a period of six years, of *M. audouini* infection in which the production of fluorescent hairs was delayed, though typical cultures were obtained. In these cases, as in the present case, the hair infection was confined to a simple mycelial invasion with no external spore sheath production. However, in the other cases fluorescent hairs were visible after about one month and then a typical spore sheath was found. The appearance of the hairs in our case suggests an attenuated infection.

CASE 2.—A girl aged 5 first seen on 28.vi.54 had a large patch of non-inflammatory tinea capitis on the left frontal area. The stated duration was one week. There was no fluorescence under Wood's light: the peripheral hairs showed no fluorescence of the intrafollicular parts of the hair. She was given Procelium Cream (Genatosan) for local application and hairs taken for mycological investigation. Two weeks later there was no change. Treatment with Asterol Cream (Roche) was started. On 19.vii.54 there was still no change and further hairs were taken for examination. On 2.viii.54 the condition was quite inactive and no hair stumps were found, and again on 9.viii.54 no signs of active infection were discovered. Both cultures from this child yielded *M. canis*.

CASE 3.—A girl aged 8, a sister of Case 2, was first seen on 28.vi.54 with non-inflammatory tinea capitis on the occipital part of the scalp. The infection had been present for one month. Under Wood's light the infected hairs were dull grey but there was no fluorescence. Manual epilation of peripheral hairs also failed to reveal fluorescent intrafollicular hair shafts. Hairs were taken for culture at the first attendance but were negative microscopically and culturally. She was given Procelium Cream (Genatosan) and later Asterol Cream (Roche) for local application. On 8.vii.54 there was no clinical change and still no fluorescence under Wood's light, but on 19.vii.54 brilliant green fluorescence was observed in a large number of hairs. A further culture of hairs taken on this later date yielded *M. canis*. On 2.viii.54, only fourteen days later, a tiny fluorescent stump was the sole remaining evidence of infection and was removed with forceps. On 9.viii.54 the area showed no evidence of active ringworm infection.

There was nothing in the mycological findings in connection with either Case 2 or Case 3 to suggest anything unusual about the infection. In the direct microscopical examination both the fluorescent and the non-fluorescent infected hairs showed the characteristic ectothrix sheath of small polyhedral spores measuring from 2 to 4 μ (though the majority were between 3 and 3.5 μ), and arranged in mosaic pattern. On several different culture media, cultures developing from the fluorescent and the non-fluorescent hairs showed no significant differences, and both were of the characteristic orange-pigmented *M. canis* type. There was abundant production of macroconidia in all the cultures sown from both fluorescent and non-fluorescent hairs, and these were of the usual type—fusiform, multilocular with decorated external walls and varying in length from 62.9 to 88.8 μ .

In fact, there was no significant difference between the Wood's light positive and the Wood's light negative infected hairs in the cases of these two children: or between these and the fluorescent hairs of other cases of *M. canis* infection both from Northern Ireland and from different parts of England.

DISCUSSION.

The phenomenon of fluorescence of ringworm infected hairs, discovered by Margaret and Devèze (1925), was attributed by them (1929) to the fungus itself. Vigne (1927) thought that the fluorescence was due to the presence of spores arranged in a cluster around the hair shaft. Davidson and Gregory

1932) and Gregory (1935) attributed the fluorescence to the hair rather than the fungus. This is now accepted. Robinson *et al.* (1953a) have investigated the chemical nature of the fluorescent substance and shown that it is a small molecule which resembles a peptide and contains a $-\text{CONH}-$ group, a $-\text{OH}$ group, $-\text{CH}_3$ group, and a $=\text{NH}$ group". This substance may be extracted from infected hair by boiling in distilled water and it dries to a fine powder which retains fluorescence when exposed to Wood's light.

These authors have also shown (1953b) that when infected hair is removed from the scalp viability of the fungus will eventually be lost but fluorescence will be retained. This observation fits in with the practical aspects, since when a fluorescent tinea capitis is clearing spontaneously it is not possible to obtain a sensitive culture when *all* fluorescence has disappeared.

On the other hand, early in the infection there seems to be a stage when the hair has been invaded and the fungus can be recovered in culture but before the fluorescent material has been produced, and this is usually before the development of the external spore sheath. In our Case 1 no external spore sheath was ever found and presumably the infection was, for some reason, attenuated before this could develop.

The two sisters (Cases 2 and 3) with *M. canis* infection are particularly interesting because they were first seen together on the same day, both attended the same school and can reasonably be regarded as having either infected one another or been infected from the same source. Yet on their first attendance neither showed fluorescence and *Trichophyton sulphureum*, which is now the most common cause of tinea capitis in Northern Ireland (Beare, 1954), was suspected. Case 3 eventually, after a delay of three weeks from first attendance, and seven weeks from the estimated onset of infection, did show fluorescent hair stumps but her sister cleared without ever having fluorescent hair stumps at any time. The short duration in both cases, suggesting an avirulent type of infection, is noteworthy.

Whittle (1953) recorded an outbreak of tinea capitis due to a dysgonic type of *M. audouini*. It was characteristic of this outbreak that cure was obtained quickly; on the average, only nine months and x-ray epilation was employed in only 4 of the 13 cases. Whittle (1954b) points out that in several of these cases there came a time when it was not possible to say from the appearance in Wood's light whether the infection was still present or not and microscopic examination was necessary.

Microsporum gypsum infections of the scalp have not been observed in Northern Ireland. The literature with regard to fluorescence in these infections is contradictory. Wilson and Plunkett (1951) state that it is usually applied that *M. gypsum* does cause fluorescence but they themselves deny this and Dalton *et al.* (1950) quote case reports with no fluorescence. Trice and Shafer (1951) describe 4 cases of tinea capitis due to *M. gypsum*, 3 of which

did not fluoresce but 1 did. Gonçalves (1953) recorded 3 scalp infections which did show fluorescence. Whittle (1954a) recorded an outbreak of *M. gypseum* infections in East Anglia but there were no scalp infections.

CONCLUSIONS.

Non-fluorescent *Microsporum audouini* and *canis* scalp infections have been observed. This is exceptionally rare.

Non-fluorescence may be confined to avirulent types of infection, and available evidence suggests that differences in the host rather than in the fungus are responsible for these minimal infections.

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ANGIOKERATOMA CORPORIS DIFFUSUM.

J. H. PRICE, M.B., CH.B.,

The University Department of Surgery, The Royal Infirmary,
Manchester.

IN 1898 Fabry described a condition which he named purpura haemorrhagica nodularis in which hyperkeratotic pin-head purple spots were disseminated over the skin of the body. Biopsy showed these lesions to be in the skin papillae and to consist of dilated capillaries surmounted by hyperkeratotic epidermis.

Only twenty cases of this disease, which Fabry later renamed angiokeratoma corporis diffusum, were recorded before 1939, when Ruiter published the case histories of three brothers in whom cardiovascular and renal abnormalities were associated with the typical skin lesions. These patients also suffered from pains in the hands and feet, oedema of the lower limbs, and mild hypertension. One of these patients died in uraemic coma and at autopsy the most striking pathological lesion was a great thickening of the muscular layer of the arterial walls in the kidneys, adrenals, liver, spleen, lungs, heart and brain. On microscopy, vacuolation of the muscle cell cytoplasm in the tunica media of these arteries was found.

In 1951 Scriba and Kühnau demonstrated ten times the normal amount of lipid related to sphingomyelin in the arterial muscle cells. Further detailed study revealed this doubly refractile diaminophosphatide in the ganglion cells of the brain, in peripheral nerves, myocardial cells, Kupfer cells of the liver, and in the foam cells of lymph nodes. Because of the widespread deposition of the lipid, Scriba suggested that angiokeratoma corporis diffusum was a lipid storage disease similar to Niemann-Pick's disease.

The following case is reported because of the rarity of the condition and because there were some unusual associated defects of growth.

CASE REPORT.

A twenty-three-year-old fitter's labourer was originally referred to hospital because of a rash on his buttocks, abdomen and scrotum which had been present as long as the patient could remember. It was non-irritant, and the patient's main complaint was of attacks of pain in the fingers and toes, described as "stinging and burning". The pains first occurred in the toes at the age of 10 years and appeared every time he attempted to run or play games. On resting they disappeared completely within a few minutes. His feet had never perspired and in the summer he could not go to

school in his bare feet, as his brothers did, because of tender soles ~~and the~~ pains in his toes.

He also complained that his feet were swollen, particularly during warm weather when he was compelled to wear larger shoes than usual.

When he was 15 years old similar stinging pains "like pins and needles" occurred in the fingers. They were brought on by rapid changes in environmental temperature and when he lifted heavy weights. These attacks gradually became more frequent until at the age of 21 he had to leave his job as a boilermaker's apprentice because the heat at work made his pains so severe. Cooling the fingers and toes, with rest in bed, relieved the pains.



FIG. 1.—Close-up view of the skin over the lumbar spine. The angiomas are only partly hyperkeratotic and vary from pin-point blue-red spots to a larger purple-black papular form.

There was no previous history of illness or injury. He was the fourth of six brothers, all of whom were 5 ft. 10 in. in height, whereas he was 5 ft. 3 in. tall. His mother's brother was afflicted with tingling pains in his feet and died of renal disease at the age of thirty-five. It was not known whether or not he had a skin lesion.

On examination.—He was a pale Irish lad of squat build. The outstanding features of his appearance were the skin lesions, the short thick neck and the prominent clavicles, which were abnormally thick in their whole length. His high-pitched voice, light beard and height of 5 ft. 3 in. gave him a striking resemblance to a boy of about 15 years. The skin was dry and coarse with a rash covering the back of the trunk and thighs and extending round the flanks on to the abdomen and chest. It was most dense over the lumbar spine and both iliac crests. The eruption consisted of small slightly elevated papules varying in colour from blue-red to purple-black and from pinpoint to 3 mm. in diameter (Fig. 1). The skin at the umbilicus was leaden-hued and hyperkeratotic, clustered with papules up to 5 mm. diameter. The scrotum also was covered with these larger papules but the hands, feet, head and neck were completely spared. The colour did not fade on diascopic pressure.

Rotation of the shoulders and extension of the elbows and fingers were limited, the latter giving him a mild degree of claw hand. He had bilateral pes planus and the ligamentum nuchae was abnormally thick. Pubic hair and the external genitalia were normal. Spontaneous penile erections occurred, but no emissions. Axillary hair was very scanty and he shaved only once a week because of the light beard. No abnormality was found on clinical examination of the heart, lungs and abdomen. B.P. 120/125/75/80 on repeated readings. There was, however, persistent ankle oedema and the feet were constantly dry even in a hot environment. Nutritional lesions were absent from the fingers and toes, and the pulses at wrist and ankle were normal. The reactive hyperaemia test was normal for the hands. The only abnormality on repeated examination of the central nervous system was a slight blunting to pin-prick in the fingers and toes distal to the proximal interphalangeal joints. Fundi were normal. Vision was good and there was no corneal opacity.

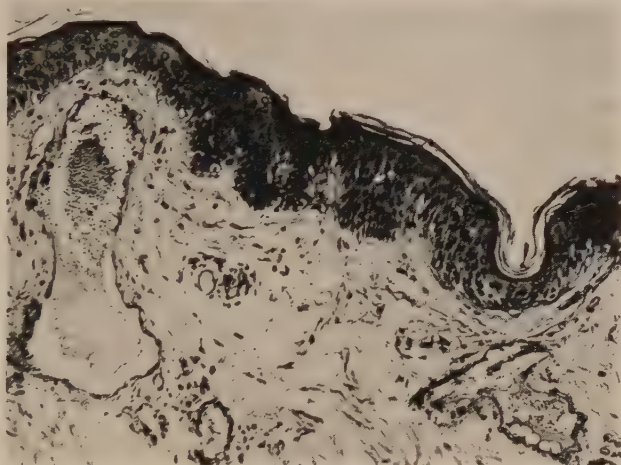


FIG. 2.—Skin from the left iliac crest showing two blood-filled spaces in the dermis. There is slight hyperkeratosis. H. and E.

Investigations.—Blood count: Hb. 86%, C.I. 0.94, W.B.C. 5,700 (Polys. 55%; Lymphos. 21.0; Large monos. 6.5; Eos. 2.5; Basos. 0.5%). Platelets 258,000. Urine: No albumen or sugar. Microscopy: Epithelial cells, a few red blood cells, granular casts.

Blood urea 20 mg./100 ml.

Urea clearance 100% of average normal.

Liver function tests: Serum albumen 4.0; serum globulin 2.7; thymol turbidity units; alkaline phosphatase 10.0 units/100 ml.

S.C.G. normal.

W.R. negative in blood and C.S.F.

S.F. contained R.B.C. 750 c.mm., polys. 2 c.mm., lymphos. 10 c.mm. Other normal. Serum calcium 9.4 mg. 100 ml. Serum phosphorus 4.4 mg. 100 ml. Ionized calcium 180 mg. 24 hour urine (normal up to 400 mg.). 17-ketosteroids (urine) 4.8 mg. 24 hours. Gonadotrophins (urine) less than 9 m.u. 24 hours. (Normal 12-30 m.u.) Electrophoretic plasma protein and lipid patterns were normal.

Roentgenograms.—Chest: Normal lung fields and cardiac shadow. Clavicles unusually thin in their whole length with a normal ratio of cortex to medulla. Cervical spine:

The bodies of the vertebrae are reduced in height and show a double contour. There is a relative increase in width of the disc spaces. Dorsal spine and pelvis normal. Skull normal. Teeth normal. The radial and ischial epiphyses have not fused completely.

Histology.—(Skin of buttock.) Sections show slight hyperkeratosis, a little more marked over the occasional dilated capillary channels found in the papillary layer (Fig. 2).

A section of pectoralis major muscle shows no abnormality. There is, however, one muscular artery in which there is marked vacuolization of the cytoplasm of the cells of the media (Fig. 3). There was unfortunately at that time insufficient biopsy material for the demonstration of phospholipids.

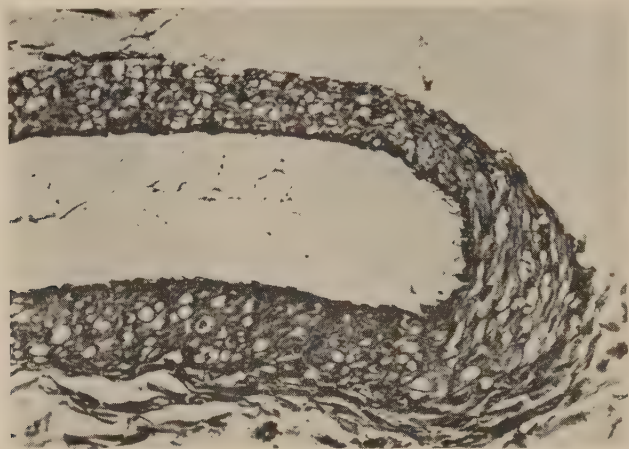


FIG. 3.—A muscular-walled blood vessel showing swollen muscle cells of the tunica media with vacuolization of cytoplasm. H. and E.

DISCUSSION.

The patient detailed in this paper has many features in common with those previously described under the heading of *angiokeratoma corporis diffusum* (see Table I). Typical of the condition are the skin lesion, the physical weakness, unusual limb pains without vascular abnormality, ankle oedema, disturbed sweat secretion and urinary abnormalities. There are, however, additional features. The most striking of these are the stunted growth with adequate muscle bulk, together with an abnormal cervical spine, hypertrophied clavicles and joint contractures.

The vacuolation of the arterial muscle is similar to that described by Scriba and is possibly part of a generalized lipid disorder in which a diaminophosphatide related to sphingomyelin involves many body tissues. This, together with the mesenchymal dysplasia and family history, suggest an inborn hereditary defect as the causative factor.

My thanks are due to Professor A. M. Boyd and Dr. Twiston Davies for permission to publish this case report, and to Professor R. P. Jepson for his help in its preparation.

TABLE I.

	Fabry (1898).	Sibley (1918).	Taguchi (1938).	Weicksel (1925).	Stimpke (1916).	Steiner and Vörner (1909).	Robba (1937).	Anderson (1898).	Ruiter (1953) 1.	Ruiter (1953) 2.	Ruiter (1953) 3.	Kooy (1953).	Seriba (1951).	Price.
Physical weakness and diminished capacity for work	..	+	+	+	..	+	..	..	+	..	..	..	..	+
Spasms or cramps in the hands and feet	..	+	..	..	+	+	..	..	+	+	+	+	..	+
Periosteal oedema	..	..	..	..	..	..	..	..	+	+	+	+	..	+
Hypertension	..	+	..	..	..	+	..	..	+	+	+	+	..	..
Turbid sweat secretion	..	..	..	..	..	..	..	..	+	..	..	..	..	+
Corneal opacity	..	..	..	+	..	..	..	..	..	+	+	..	..	..
Secondary abnormalities:														
Albuminuria	..	+	+	..	..	+	+	+	+	+	+	..	+	..
Leucocytes	..	+	..	..	..	+	..	+	+	+	+	..	..	..
Red cells and casts	..	+	..	..	..	+	..	+	+	+	+	..	..	+
Growth defects (see text)	..	..	..	..	..	..	..	..	..	..	..	..	..	+

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Scleredema.—Dr. P. D. SAMMAN.

Mr. A. S—, aged 58.

This man, a diabetic who has received insulin treatment for 23 years, recently noted that his neck was getting bigger and needed a larger size in collars. He has had no other symptoms and no recent acute illness.

Examination shows thickening and hardening of the skin of the back of the neck and spreading down over shoulders, greater part of chest and upper arms, and also the upper thighs. The distal parts of the extremities are spared. The edge is ill-defined. The surface is a little redder than the normal skin.

Biopsy from the back of the shoulder was made to a depth of $\frac{5}{8}$ in. but failed to reach the subcutaneous tissues. Histologically this consists of a very thin layer of epidermis and the remainder is due to a great increase in collagen. There are few adventitial structures present.

Clinically the appearances are those of scleredema of Buschke but without a typical history at the onset.

I am indebted to Dr. Dudley Hart for permission to show this patient.

Fibrosarcoma of Multicentric Origin.—Dr. R. G. HOWELL (for Dr. G. B. MITCHELL-HEGGS).

Mr. V. G—Jamaican negro, aged 24.

History.—In September 1953 the left big toe became painful and swollen, and ulcerated in December 1953. During this time a nodule appeared on the dorsum of the left 4th toe, and several lesions superficially resembling plantar warts occurred on the left anterior arch. In the past month the left 5th toe has become painful, and has developed nodules which have ulcerated.

Previous History.—Yaws treated by injection ten years ago.

On Examination.—Left foot : The left big toe is swollen generally and ulcerated on the medial side ; the nail is opaque and becoming detached from the nail bed. There are several fleshy nodular outgrowths on the plantar surface of the toe. On the 4th and 5th toes are similar nodules, some of which are ulcerated. On the sole of the foot are several lesions superficially resembling plantar warts, but some of them have a fleshy appearance and are becoming nodular. The lesions on the big toe at first resembled warts. Behind the left thigh there is a group of 3 or 4 hard nodules, deep to and attached to the skin.

Otherwise the general health is good. There are no enlarged glands, and no abnormal findings in any other system.

Investigations.—Haemoglobin 100%. W.B.C. 6000. Polymorphs 56%, eosinophils 1%, lymphocytes 41%, monocytes 2%.

Blood W.R. : Negative. Kahn : Negative.

Treponemal immobilization test : positive.

Skiagram of chest.—No pulmonary lesions seen.

Skiagram of left foot (available).—Considerable bone reabsorption affecting the terminal phalanges of the 1st, 4th and 5th toes. There is no periostitis and no new bone formation. This suggests an infective necrosis secondary to the skin changes.

Examination of nail scrapings showed no fungus.

Urine.—N.A.D.

Blood Uric Acid.—3.1 mg./100 ml.

Biopsy of lesions on 1st and 4th toes and behind left thigh. The general histological picture is that of a fibrosarcoma of a low grade of malignancy. The cells are plump, irregularly arranged fibroblasts with little nuclear variation and infrequent mitotic figures. The lesions appear to be expanding and in a few places possibly invasive.

The two lesions are proceeding (or have proceeded) to ulceration; the thigh nodule is considerably deeper and there is an increase in normal collagen in the overlying dermis with corrugation of the epidermis (Dr. M. V. Salmon for Prof. Newcombe).

Comment.—This patient was seen by Sir George MacRobert who thought that the clinical appearance might result from tertiary yaws, especially as the treponemal immobilization test was positive. However, the histological picture was not compatible with this and resembled a fibrosarcoma.

The diagnosis of Kaposi's haemorrhagic sarcoma was also considered, but was dismissed on the histological appearance.

There does not appear to be any case of multiple fibrosarcomata recorded in the literature. Gentele recently reported a series of 129 cases of fibrosarcoma and Heller a series of 60 cases without any example of multiple tumours.

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GENTELE, H. and HOLMGREN, H. (1951) *Acta. dermat. venerol. Stockh.*, **31**, 322.

HELLER, E. L. and SENTURIA, H. R. (1950) *Surgery*, **27**, 673.

Postscript.—Treatment with penicillin, 2 million units daily for 14 days, made no change in the lesions.

DR. A. N. P. MILNER: Some years ago, while working on the Gold Coast, I saw a great number of these cases. In my opinion this case is clinically tertiary yaws. The morphology of the condition appears to me to be quite typical, and the situation of the lesion on the feet, is one on which the lesions of tertiary yaws are commonly found.

The following cases have been published in *Proc. R. Soc. Med.* **47**, 1061.

Lymphocytoma.—Dr. J. S. PEGUM.

Eosinophilic Granuloma (Erythema Elevatum Diutinum Type).—Dr. ARTHUR PORTER.

Purpura Cryoglobulinaemica.—Dr. N. A. THORNE for Dr. BRIAN RUSSELL.

Dermatomyositis (Sclerodermatous Phase).—Dr. STEPHEN GOLD.

The following cases also were shown:

Juvenile Dermatitis Herpetiformis (Two Cases).—Dr. BRIAN RUSSELL.

Keratolymphangioma.—Dr. P. J. FEENY.

Kaposi's Idiopathic Haemorrhagic Sarcoma (Responding to Penicillin).—Dr. STEPHEN GOLD.

Acrodermatitis Enteropathica.—Dr. I. S. HODGSON-JONES.

Hyperkeratosis Follicularis et Parafollicularis in Cutem Penetrans (Kyrle) with Lesions of the Palms and Soles.—Dr. K. V. SANDERSON.

SOUTH WEST OF ENGLAND AND WALES DERMATOLOGICAL SOCIETY.

Bristol, October 1954.

Pustular Psoriasis Treated with Cortisone and A.C.T.H.—Dr. L. TULLOCK
for Dr. R. P. WARIN.

A telegraphist, aged 50.

History.—In November 1953, this man developed typical psoriasis, involving mainly the limbs. In March 1954, there appeared on the fingers an eruption indistinguishable from dermatitis repens, accompanied by thickening of the nails and loss of some of them. This was followed a few weeks later by a crop of sterile pustules, beginning on the hands and eventually covering most of the body surface. During phases of acute activity there was pyrexia.

Treatment.—A short course of cortisone, averaging about 75 mg. daily, produced little effect, but later cortisone in a dosage of 200 mg. daily resulted in a dramatic improvement and the skin became almost clear. The condition relapsed on reducing the dose to 100 mg., but improved again rapidly on raising it to 200 mg. once more. After about one month, on a maintenance dose of 125–150 mg., a gradual worsening of the condition became apparent. This was reversed when the daily dose of cortisone was reduced to 37.5 mg. and 40 mg. of ACTH was given in addition. At present the skin is almost completely free from pustules on 50 mg. of cortisone and 40 mg. of ACTH daily.

Investigations.—Blood W.R. and Kahn, negative. Blood count, normal.

Chest skiagram, normal.

Histology.—Forearm: parakeratosis, hypertrophy and oedema of rete pegs, slight perivascular lymphocytic infiltration of dermis.

Comment.—The features of special interest in this case were the progression clinically from psoriasis, through dermatitis repens, to generalised pustular psoriasis, and the striking response to large doses of steroids.

Herpes Simplex Generalisatus with Keloid Formation.—Dr. M. HEWITT for Dr. R. P. WARIN.

A baby, aged 15 months.

She was a premature baby, delivered at 33 weeks by Caesarian section. The birth weight was 4 lb. 7½ oz. Rearing was uneventful.

At the age of 10 months she was admitted to hospital with acute gastroenteritis and moderate dehydration: the haemoglobin was 54% and *B. proteus vulgaris* was isolated from the faeces. She responded well to sulphasuccidine and an intravenous transfusion of 500 c.cm. of dextrose-saline.

Ten days after admission an eruption developed on the lips and buccal mucosa which was immediately followed by a vesiculo-bullous eruption on the abdomen, buttocks, hands, arms, legs, back and finally the face. The individual lesions were discrete, ruptured within a few days and were followed by ulceration. On healing there were well-defined scars and many of these developed large pink keloids. The vesicles continued to erupt in diminishing numbers during the ensuing six months. Some of the keloids have spontaneously disappeared.

Five weeks after admission the infant developed swelling of the right side of the face and also of the right wrist and hand. Skiagram revealed osteomyelitis at the lower end of the radius. Pus was aspirated.

Investigations.—At the height of the eruption the blood count was: W.B.C. 6200 per c.mm.; eos. 1%; segmented neutros. 32%; metamyelocytes 2%; lymphos. 56%; monos. 9%.

The fluid from a bulla was examined microscopically and revealed only debris and very scanty staphylococci. Culture was negative.

Comment.—Herpes simplex running such a protracted course was described by Cohen (*J. Amer. med. Ass.*, 1916, **66**, 1598).

Atrophie Blanche (Two Cases).—Dr. R. P. WARIN.

CASE 1.—A machinist aged 21.

History.—Six months ago he bruised the back of the left lower leg. A brown area developed and spread to the ankles, feet and to the opposite leg. Three months ago ulcerated areas developed below the internal malleolus.

Past and family history negative.

Examination.—Over the dorsa of the feet and toes and just below the ankles are patches of pigmentation and numerous 0.2–0.4 cm. circumscribed pale pink slightly depressed areas. Patches of brownish pigmentation are also present over the legs and lower thighs. The skin of the feet is cold and sweaty.

Investigation.—Blood count and sedimentation rate, normal. Blood W.R. and Kahn, negative. No abnormal capillary fragility demonstrated in arms. Skiagram of chest, normal.

Histology.—Perivascular round-cell infiltration: necrotic lesions in media of arterioles; new capillaries.

CASE 2.—An engraver aged 17.

History.—For three years lesions have been evident around the ankles and on the dorsa of the toes and adjacent parts of the feet. Ulceration has occurred in both areas from time to time.

Past and family history normal.

Examination.—Over the dorsa of the toes and adjacent parts of the feet and below the ankles are patches of pigmentation, and numerous 0.2–0.4 cm. circumscribed pale pink slightly depressed areas, some ulceration and scars.

The skin of the feet is cold and sweaty.

Investigation.—Blood count and sedimentation rate, normal. Blood W.R. and Kahn, negative. No abnormal capillary fragility demonstrated in arms. Skiagram of chest, normal.

Histology.—A little round-cell infiltration. New vessels and connective tissue.

Comment.—Both these young men show lesions around the malleoli which have the appearance described as atrophie blanche by Milian and later by Gonin (1950). They have both had areas of pigmentation over the legs showing features of Schamberg's disease. In addition, both have had patches over the junction of the dorsum of the feet and toes which show numerous circumscribed atrophic areas 2–4 mm. across.

Both patients have cold sweaty feet.

In spite of the sex, youth, large patches of pigmentation, the unusual distribution of the lesions on the foot and absence of severe pain, I believe that the condition must be closely related to atrophie blanche.

Dr. J. MARTIN-SCOTT: The fact that one of these patients had been taking occasional adalin may be of significance in regard to the pigmentation.

Dr. I. WHIMSTER: This histology, including the formation of new capillaries, is that which occurs when the capillary pressure is raised, as for example in association with the "ankle blow-out syndrome" (Cockett and Jones, 1953). The clinical picture of atrophie blanche may be the first manifestation of the ankle blow-out syndrome and it is possible that in these cases a similar abnormal communication between the deep and superficial veins occurs in the dorsum of the feet and toes.

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 COCKETT, F. B. and JONES, D. E. E. (1953) *Lancet*, i, 17.

OBITUARY.

DR. J. M. H. MACLEOD.

Dr. J. M. H. MacLEOD was 84 when he died at his home in Farnham on 10 December 1954. His death almost closes a great era of British Dermatology which covered roughly the first third of the twentieth century. Of those famous dermatologists of that neo-Georgian period none should stand higher than MacLeod as a clinician, student, writer and as a personality. The gap he leaves in British Dermatology will not easily be filled.

John MacLeod Hendrie MacLeod, the son of John Balmain MacLeod, M.D., of Dundee University, was born at Galston, Ayrshire, in 1870. After graduating M.A. at St. Andrews he studied medicine at Aberdeen, qualifying M.B., C.M. in 1894, and took the M.D. (Honours) in 1898. His next move, a typically Scottish one, was to London where he took the M.R.C.P. in 1900. He was elected to the Fellowship of the Royal College of Physicians of London in 1916.

In what he himself called "Milestones on a Dermatological Journey", the title of the Prosser White Oration which he delivered before St. John's Hospital Dermatological Society in 1948, he describes his studies abroad at the clinics of such distinguished teachers as Hebra, Kaposi and Ehrmann in Vienna, Lassar in Berlin, Unna in Hamburg, and "most inspiring of them all, Paris with Ernest Besnier". On returning to London he established in small laboratories at Charing Cross Hospital Medical School and at his house in Harley Street, courses of histology and pathology which he describes as "fairly successful". The fact that, in addition to stimulating many of his colleagues in this country, students from across the Atlantic, among them the late Howard Morrow and Oliver Ormsby, were attracted, speaks for their value. Another result of these courses was the publication in 1903 of the *Practical Handbook of Pathology of the Skin*. The excellence of this book, in which nearly all the illustrations were drawn by MacLeod himself, who also personally cut, mounted and stained all the preparations with his own hands, made it almost unique in this country. A second edition was published, in collaboration with Dr. I. Muende, in 1940.

In 1901 MacLeod was appointed assistant to Dr. (later Sir) James Galloway at Charing Cross Hospital, one of the last physicians to combine the appointment of general physician with that of dermatologist at a London teaching hospital. When these two functions were separated in 1914 MacLeod was appointed Physician for Diseases of the Skin and Lecturer on Diseases of the Skin to Charing Cross Hospital and Medical School, and he held this appointment until 1930. In 1903 he became Physician for Diseases of the Skin to The Victoria Hospital for Children, Tite Street, Chelsea (relinquishing this in 1923), and in 1906 he was appointed Physician and Lecturer in Diseases of the Skin to the London Hospital for Tropical Diseases. In 1923 he was appointed Consultant Physician for Skin Diseases to the Metropolitan Asylums Board: in this his chief activity was looking after the Goldie Leigh Homes for Children, where in conjunction with Dr. S. Cochrane Shanks he carried out much of the good work which made ringworm of the scalp in children almost a rare disease in London by the time he retired in 1936. The Metropolitan Asylums Board was absorbed by the London County Council and later by the Ministry of Health, but the good work MacLeod did there is still carried on and his name not forgotten.

In 1923, on the re-formation of the London School of Dermatology with its parent hospital St. John's, the reputation of which was not very high in dermatological circles at that time, MacLeod became Honorary Director of Pathology to that hospital and school. Here his organizing ability and his stimulating zest for hard work transformed the pathological work of the hospital and its attached school. Out of that school has evolved the present Institute of Dermatology of the British Postgraduate Medical Federation, still housed at, and in close collaboration with, St. John's Hospital for Diseases of the Skin: for the subsequent development of the Institute much credit

naturally goes to MacLeod, and it is intended to recognize this by naming the pathology laboratories after him.

MacLeod's connection with the Homes of St. Giles for British Lepers where he first worked with, and later succeeded, the late Sir Malcolm Morris as Chairman and Medical Director was long and intimate. His great interest in this still undefeated disease appears to have been stimulated by his being asked, as official delegate of the School of Tropical Medicine, to open the discussion of the pathology of the disease at the Second International Congress on Leprosy held in Bergen in 1909. His experience of that congress is most entertainingly described in the Prosser White Oration already noted.

MacLeod took an active part in the meetings of dermatological societies, both at home and abroad. He was an original member of the British Association of Dermatology and Syphilis, being Secretary in 1926 and President in 1930. He was elected an Honorary Member in 1951. He was a member of the Dermatological Section of the Royal Society of Medicine and President in 1927: Vice-President of the Dermatological Section of the British Medical Association in Aberdeen and President at the Bradford Meeting in 1923. He joined St. John's Hospital Dermatological Society in 1932, becoming President from 1932-34, and being elected Honorary Life Fellow in 1949. His recognition abroad is shown by his being a Corresponding Member of the American and Danish Dermatological Societies and of the *Société Française de Dermatologie*. He was also an Honorary Member of the Japanese Society of Dermatology and Syphilis.

MacLeod's writings were numerous and varied, but always characterized by clarity and simplicity of style. His text-book *Diseases of the Skin* published in 1930 and reprinted with a supplement in 1933 was the most comprehensive and complete book published in this country at the time. Although now it would be said to be somewhat out of date, it is still a monument of clear and accurate description which, from its author's facile style, is so essentially readable. His *Practical Handbook of Pathology of the Skin* has already been mentioned and in 1918 he wrote of *Burns and their Treatment* as the result of his experiences as consultant in skin diseases to the Royal Flying Corps.

His contributions to current journals were numerous and varied. Naturally, most were to this Journal from 1898 to 1928, but he contributed also to many other journals both at home and abroad.

MacLeod was a man of wide cultural interests, widely read, and appreciated pictures, china and old furniture. He was no mean craftsman, woodwork being his chief interest. He was a keen yachtsman, angler and shot, and nothing pleased him more than to take a carefully selected party sailing among the Hebrides in the "Kittiwake".

He was a great host, thoroughly enjoying entertaining his guests and being the liveliest member of the party.

He was genuinely one of nature's gentlemen and could well "walk with Kings" and not "lose the common touch" as exemplified in his private as well as in his hospital practice.

In his teaching he abhorred verbosity, padding and slipshod work of any kind. To the last his mind remained as clear and incisive as ever in spite of physical hardships.

Many will remember his taking up a strategic position in the sunshine on the steps of Bedford College during the Tenth International Congress of Dermatology, where his many friends and past students from different parts of the world delighted to gather round him.

He was an active and honoured member of the Clan MacLeod, and President of the London Branch of the Clan MacLeod Society in 1947. A magnificent sight was his leading the entrance with Dame Flora at the annual gathering of the Clan in 1947.

In 1897 he married Eva, daughter of Joseph Ruston M.P. for Lincoln, who survives him with a son and daughter. To them and to his grandchildren we extend our most sincere sympathy.

BOOK REVIEWS.

LIGHT SENSITIVITY*

TWO-THIRDS of this book on photosensitization and protection against light is a review of the subject, and the last part is an account of the authors' experiments. Photosensitization has its uses in ameliorating or curing certain skin disorders by intensifying the reaction to therapeutic irradiation. The authors find that the best local protectors of the skin against injurious action to light are those substances that sensitize the skin when taken internally, e.g. an ointment containing eosin will prevent solar erythema and haematoporphyrin will avert any destructive action from exposure to light in those who have been sensitized by the porphyrins. Haematoporphyrin is particularly useful because it absorbs a wide band of the spectrum. When used to increase the sensitivity to light in patients with psoriasis, alopecia areata, acne vulgaris, leg ulcers etc. it is injected intravenously half an hour before irradiation, 1 ml. of a 0.2% solution in saline. The same concentration absorbed on to talc was used in the following protective ointment: Paraffin. molle 10 g; Lanolin 10 g; Porphyrinized talc 5 g.

The experimental part is well illustrated: there is a bibliography but no index.
G. W. B.

ECZEMA.†

THIS volume is the report of a symposium on the subject of eczema held at Marseilles in October, 1953. Most of the leading members of the French Society of Dermatology and Syphilology, and several visitors from abroad, read papers or contributed to the discussion of them.

The more important communications included the histology of the early lesion (Meischer; Charpy; Civatte), patch testing (Tzanck and Sidi; Charpy and Castelain), the mechanism of sensitization (Sulzberger and Witten; Charpy and Oddoze), the role of micro-organisms in eczema (Storck), and the part played by the nervous system in the eczema reaction (Charpy and his collaborators).

Eczema devoid of controversy might make dull reading, but there is no lack of interest in these pages. Inevitably there is disagreement, not only about the initial eczematous lesion, but also about the interpretation of patch tests, histological sections, the results of animal experiments, and the very nature of eczema itself. The dermatologist who finds no problems in this subject need not read this book; to all others it is strongly recommended.
H. T. H. W.

* *Fotosensibilizacion y Fotoproteccion*. By M. M. TINA0 and A. Z. VIDAL. (1954). Zaragoza: Institution "Fernando el Catolica". Pp. 135.

† *Le Mécanisme Physio-Pathologique de l'Eczéma*. By JACQUES CHARPY (1954). Paris: Masson & Cie. Pp. 288, figs. 65 and 11 plates.

CURRENT LITERATURE.

STUDIES IN PALLESTHESIA : DEPRESSION OF VIBRATORY SENSE LEVELS IN LUPUS ERYTHEMATOSUS. S. GOLDBLATT. (1954) *J. invest. Derm.*, **22**, 97.

Three patients recorded as having had normal vibration sense before having L.E., presented pallypnoesthesia when at last they got it. Cyanocobalamin otherwise known as vitamin B₁₂ enhances cutaneous appreciation of vibration and is therefore the best treatment for L.E. When it fails it is because one of a number of other states (which includes chronic nicotine poisoning) is also present.

J. H. T. D.

EXPERIMENTAL CONTACT DERMATITIS. I. DINITROCHLOROBENZENE CONTACT DERMATITIS IN GUINEA PIGS. I. ZELIGMAN. (1954) *J. invest. Derm.*, **20**, 109.

The author, after briefly reviewing the literature, describes the experiments which have led him to conclude that to the skin of the guinea-pig concentrations of 1% DNCB in acetone and of 0.1% in petrolatum are primarily irritant, and that evidence for or against the capacity of DNCB to sensitize the skin of guinea-pigs is hard to come by.

He also describes the histological changes brought about in guinea-pig skin by great and small concentrations of this reagent.

J. H. T. D.

PERFUSION OF ISOLATED DOG SKIN. A. R. KJAERGAARD. (1954) *J. invest. Derm.*, **22**, 135.

The difficulty about perfusion has always been that of finding a large enough piece of skin supplied by a single artery. But from the thigh of a large dog it is possible, by using the technique described, to obtain 70 sq. cm. supplied by a single branch of the saphenous artery.

J. H. T. D.

BARBITURAL CONCENTRATIONS IN THE SKIN AND HAIR OF GUINEA PIGS. R. W. GOLDBLUM, L. R. GOLDBAUM and W. N. PIPER. (1954) *J. invest. Derm.*, **22**, 121.

Barbiturates may be quantitatively estimated by an ultraviolet spectrographic technique.

It is demonstrated that long-acting barbiturates, such as phenobarbitone, have a greater affinity for the skin than those of the anaesthetic type. The term "dermatitis medicamentosa" is here used for what we would call drug eruption.

J. H. T. D.

INFLUENCE OF ANOXIA ON THE DEPILATION OF MOUSE HAIR WITH X-RAYS. J. STRAUSS, A. M. KLIGMAN and S. GREENBERG. (1954) *J. invest. Derm.*, **22**, 129.

Bar Harbour C-57 mice are the best for this experiment. They have black hair growing out of white skin, and one can easily determine the phases of the hair cycle by the shading of the skin by pigment in the hair follicle. 700r is the x-ray epilation dose for mice. When the circulation is interrupted by clamping or the skin rendered ischaemic by adrenalin 1500 to 1800r are required. Similarly asphyxiated new-born mice—they can survive 20 minutes of total asphyxia—can sustain much larger quantities of total body radiation than normal ones. Certain chemical reactions to x-rays are inhibited by lack of oxygen, and it is proposed once more that the action of x-rays on the skin is one of oxidation associated with ionization of the water in tissues.

J. H. T. D.

SCLEREMA NEONATORUM TREATED WITH CORTICOTROPIN (ACTH). H. M. EISENOFF, H. A. AARON and F. C. GREEN. (1954) *J. Amer. med. Ass.*, **155**, 905.

Two infants with sclerema neonatorum treated with ACTH recovered rapidly. To one 5 mg. of ACTH was given six-hourly for 12 days and to the other 3 mg. eight-hourly for 10 days.

A. J. R.

INSECT BITES. H. V. ALLINGTON and R. R. ALLINGTON. (1954) *J. Amer. med. Ass.*, **155**, 240.

A long general review on the subject of insect bites. The processes of sensitization and spontaneous desensitization are described and the consequent variations in the lesions which may follow the bites. It is stated, for example, that newborn babies show no reaction to flea bites.

Further discussion of general aspects of the problem is followed by a brief account of insecticides and repellants. The bites of some of the commoner insects of the United States are considered in more detail. A. J. R.

TREATMENT OF DERMATOSES WITH LOCAL APPLICATION OF HYDROCORTISONE ACETATE. H. M. ROBINSON, Jr., and R. C. V. ROBINSON. (1954) *J. Amer. med. Ass.*, **155**, 1213.

The value of topical hydrocortisone acetate in the symptomatic treatment of various dermatoses is confirmed. Results in atopic dermatitis and anogenital pruritus were impressive but relapses occurred when treatment was discontinued. A concentration of less than 1% hydrocortisone acetate was relatively ineffective. A. J. R.

CHLORACNE FROM AN UNUSUAL EXPOSURE TO AROCHLOR. J. W. MEIGS, J. J. ALBOM and B. L. KARTIN. (1954) *J. Amer. med. Ass.*, **154**, 1417.

Seven cases of chloracne occurred among 14 chemical workers exposed for 5-19 months to small concentrations of the vapour of Arochlor, a chlorinated diphenyl. A. J. R.

SKIN TEMPERATURES IN PERIPHERAL VASCULAR DISEASE. T. WINSOR. (1954) *J. Amer. med. Ass.*, **154**, 1404.

A new skin thermometer is described and its clinical applications are reviewed. The instrument is simple, accurate, portable and relatively inexpensive. A. J. R.

TREATMENT OF PYODERMA WITH POLYMYXIN B-BACITRACIN OINTMENT. B. J. PASS and H. RATTNER. (1954) *J. Amer. med. Ass.*, **155**, 1153.

Polysporin, a new antibiotic ointment containing bacitracin and polymyxin B, gave promising results in 577 patients with various pyodermas. Three patients complained of a burning sensation, but there was no objective evidence of irritation. A. J. R.

SJÖGREN'S SYNDROME: REVIEW OF LITERATURE AND REPORT OF A CASE. F. E. KENNY and J. E. LONG. (1954) *J. Amer. med. Ass.*, **155**, 435.

The report of a case of Sjögren's syndrome is followed by a brief review of the literature. The author suggests that the syndrome is a manifestation of the ageing process as it affects ectodermal structures. A. J. R.

TREATMENT OF OTITIS EXTERNA WITH HYDROCORTISONE SUSPENSION. R. L. BAER and J. Z. LITT. (1954) *J. Amer. med. Ass.*, **155**, 973.

Ten cases of chronic otitis externa were treated with a hydrocortisone suspension containing Neomycin. Good symptomatic relief was obtained in most cases. A. J. R.

CLINICAL AND EPIDEMIOLOGICAL FEATURES OF AN UNUSUAL EPIDEMIC EXANTHEM F. A. NEVA, R. F. FEEMSTER and I. J. GORBACH. (1954) *J. Amer. med. Ass.*, **155**, 544.

In the summer of 1951 an outbreak of a mild exanthematic illness occurred in and around Boston. The patients were mainly children but some adults were affected. Fever of 102° F. lasting one or two days was usual, but occasionally the disease began abruptly with fever of 104° F.—105° F. The skin eruption was more profuse in children than in adults and consisted of pink or salmon coloured lesions, usually discrete, but sometimes coalescing, most marked on the face and upper chest but occasionally universal, including palms and soles. A few patients developed tiny punched-out ulcers on the soft palate or fauces. Systemic symptoms were slight or absent in children, but more severe in adults. Neutralizing antibodies could be demonstrated to transferable agents isolated from the faeces of several patients. A. J. R.

PERIPHERAL VASCULAR DISEASES AND THEIR CURE. I. MUFSON. (1954) *J. Amer. med. Ass.*, **155**, 1559.

In patients with obliterative peripheral arterial disease treatment must aim at encouraging structural dilatation of collateral vessels rather than releasing vasospasm. In the author's experience intra-arterial infusion of histamine has given encouraging results even in cases unrelieved by sympathectomy. Antibiotics can be combined with the histamine infusion in the treatment of infective complications of obliterative arterial disease. A. J. R.

ALFALFA SEED DERMATITIS. W. H. KAUFMAN. (1954) *J. Amer. med. Ass.*, **155**, 1058.

Alfalfa seeds are sometimes ingested as the result of a popular belief that they are beneficial in arthritis. The author reports two cases of patchy oedema and erythema provoked by these seeds, and mentions four additional cases that he has observed. A. J. R.

TREATMENT OF CHRONIC LEG ULCERS WITH ABSORBABLE GELATIN SPONGE (GEL-FOAM) POWDER. I. L. MILBERG and J. A. TOLMACH. (1954) *J. Amer. med. Ass.*, **155**, 1219.

Absorbable gelatin sponge in powder form was employed in the treatment of 106 chronic leg ulcers. Systemic antibiotics were given when necessary to control infection. The patients wore elastoplast dressings or elastic bandages. Good results are claimed, the ulcers healing completely in 86 patients. By paired comparison, gelatin sponge powder proved more effective than aureomycin ointment, silver leaf foil, *Aloe vera* leaf or crystalline trypsin. A. J. R.

EXTRAMAMMARY PAGET'S DISEASE OF THE SKIN. P. W. GREELEY and J. W. CURTIN. (1954) *J. Amer. med. Ass.*, **155**, 1054.

Extramammary Paget's disease has been diagnosed histologically only in the axillae and the anogenital region, both apocrine sweat gland areas. The literature is briefly reviewed and a case is reported of extramammary Paget's disease at the base of the scrotum. A. J. R.

SIMPLE METHOD OF DEMONSTRATING THE L.E. CELL BY FINGER PUNCTURE. S. ROSENFELD, A. I. SWILLER and M. MORRISON. (1954) *J. Amer. med. Ass.*, **155**, 567.

The authors have readily demonstrated the L.E. cell in 8 cases of systemic lupus erythematosus by a new and simple technique. By finger puncture 10 drops of blood are collected in a small test-tube. The blood is allowed to clot at room temperature for 4—6 hours. The clot is then broken up in the serum with a glass rod. Smears of the fluid mixture of red and white cells and serum are stained with Wright's stain and examined under the oil-immersion lens for L.E. cells. A. J. R.

A SIMPLE PROCEDURE FOR STAINING TINEA VERSICOLOR (M. FURFUR) WITH FOUNTAIN-PEN INK. M. M. COHEN. (1954) *J. invest. Derm.*, **22**, 9.

A fortune no doubt still awaits the inventor of an ink that will perform all the usual feats claimed by manufacturers. This one which is said to contain "diaminostilbene disulphonic acid coupled to two moles of 1-amino-8-naphthol 2, 4, disulphonic (Chicago) acid" should be in every dermatologist's fountain pen. J. H. T. D.

THE INHIBITION OF RESPIRATION OF CERTAIN DERMATOPHYTES BY β -PROPIOLACTONE. G. R. GALE. (1954) *J. invest. Derm.*, **22**, 1.

Not only does the presence of a piece of filter paper treated with a 1% solution inhibit the growth to the extent of 50% to 90%, but 0.5 mg. of the drug per c.c. of buffer solution greatly reduced the respiration of pieces of colony exposed to it in the Warburg manometer.

T. rubrum demonstrated its famous hardness.

J. H. T. D.

IDIOPATHIC HYPERLIPAEMIA AND PRIMARY HYPERCHOLESTEREMIC XANTHOMATOSIS:

(I) CLINICAL DATA AND ANALYSIS OF PLASMA LIPIDS. (II) ANALYSIS OF THE PLASMA PROTEINS AND LIPIDS BY MEANS OF ELECTRO-PHORESIS AND FRACTIONATION OF THE PLASMA PROTEINS; EFFECT OF HIGH SPEED CENTRIFUGATION AND OF EXTRACTION WITH ETHER ON THE PLASMA PROTEINS AND LIPIDS. (III) EFFECTS OF INTRAVENOUSLY ADMINISTERED HEPARIN ON THE PLASMA PROTEINS AND LIPIDS. W. F. LEVER, P. A. J. SMITH and N. A. HURLEY. (1954) *J. invest. Derm.*, **22** (I), 33, (II) 53, (III) 71.

Xanthoma occurs in two idiopathic states of increased plasma phospholipoid and cholesterol. It may also occur in the hyperlipaemia of diabetes or in that sometimes thought to be secondary to recurrent pancreatitis. These papers are concerned primarily with the serological differences between the two idiopathic conditions; but in connection with tables setting out details of the 41 cases of idiopathic hyperlipaemia already in the literature, and the authors' own 7 cases of that and 10 of the other thing, a clinical comparison illustrated by photographs is offered. Molecular relationships between protein and plasma lipid are discussed in relation to the findings reported.

J. H. T. D.

LIGHT SENSITIVE ERUPTIONS TREATED WITH ATABRINE AND CHLOROQUINE. J. M.KNOX, J. H. LAMB, B. SHELMIRE and R. J. MORGAN. (1954) *J. invest. Derm.*, **22**, 11.

They report substantial improvement in all 18 cases and discuss the rationale of antimalarial drugs in L.E. and eruptions provoked by light—which turns out to be what is meant by “light sensitive”. Chloroquine neither stains the skin nor causes it to fluoresce, but would, nevertheless, appear equally effective with atabrine in reducing reactions, banal or morbid, to light.

J. H. T. D.

RECOVERY OF DERMATOPHYTES FROM SHOES AND SHOWER STALLS. L. AJELLO andM. E. GETZ. (1954) *J. invest. Derm.*, **22**, 17.

Cyclohexamide is the selective germicide that enabled the authors quite easily to isolate fungi pathogenic to man from surfaces so well adapted to aspergillus, penicillin, rhizopus, mucor and scopulariopsis.

In the course of discussion the opinion emerged that pathogenic fungi are ubiquitous and ineradicable, and that attention could more profitably be directed to constitutional factors favouring their activity in the skin.

J. H. T. D.

A SIMPLE AID IN THE MICROSCOPIC DETECTION OF MELANIN. M. A. TROXELL. (1954)*J. invest. Derm.*, **22**, 5.

Recommends the use of “neutral density” filters, yellow green filters, and filters “in the 5,000–6,000 Ångstrom range” not only for the detection of melanin but for most other dermatological purposes of microscopy. If one had the filters it would no doubt be easy enough to confirm what he says, but the ordinary reader will be disappointed with the information here supplied.

J. H. T. D.

ADVANCES IN THE TREATMENT OF SKIN DISEASES. H. R. VICKERS. (1954) *Practitioner*, **173**, 373.

Dapsone (diaminodiphenyl sulphone) controls dermatitis herpetiformis very well, in doses of 100 mg. by mouth daily. The red cell count may be depressed during the first few weeks, and some patients may have slight cyanosis due to methaemoglobinaemia, but these changes tend to pass off even when the drug is continued. Mycosis fungoides has been treated, with encouraging results, with triethylene melamine given by mouth. The dose has to be determined for each patient but is usually about 1.25 mg. on alternate days. Neomycin ointment is useful in many types of pyogenic eruptions and, since it is never given by mouth, sensitization to it does not matter seriously. Mepacrine has a definite place in the treatment of lupus erythematosus. Chloroquine has been used instead of mepacrine and has the advantage of not colouring the skin. At present, it appears to be less toxic than mepacrine. Both mepacrine and chloroquine are valuable in cases of light sensitization. Hydrocortisone ointment appears to be helpful in various forms of dermatitis and particularly in pruritus ani. Monobenzylether of hydroquinone is occasionally useful in cases of pigmentation of the skin such as chloasma, although sensitization to the drug may occur. Silicones appear to protect the skin against many varieties of irritants.

A. C. R.

STUDIES IN PASSIVE TRANSFER OF SKIN SENSITIZING ANTIBODIES (ATOPIC REAGINS): THE EFFECTS OF TOPICAL ADMINISTRATION OF STEROIDS ON THE SKIN OF OLD INDIVIDUALS. M. SCHWARTZ. (1954) *Acta allergol.*, **7**, 403.

Wheals induced by passive transfer of a skin sensitizing antibody are significantly larger in older than younger subjects using the antibody in high concentration. Topical administration of oestrogen in women and testosterone in men did not affect the size of the wheals.

H. T. H. W.

CUTANEOUS MANIFESTATIONS OF ACUTE PANCREATITIS, WITH SPECIAL REFERENCE TO LIVEDO RETICULARIS. W. J. SIGMUND and W. B. SHELLEY. (1954) *New Engl. J. Med.*, **251**, 851.

They describe changes in the skin that may occur in acute pancreatitis, including morbilliform eruptions, cyanosis, jaundice, a bluish colour around the umbilicus and green oedematous patches.

The authors report a case with livedo reticularis and suggest that this and the other changes mentioned may be due to vascular damage by trypsin.

A. D. P.